TTCGATTACAGTATGACAGATACTCATTCT 3' (SEQ ID NO:53). The probe was 6FAM-CTCTGCTGTAGACGTGAACACTGTACCAATGTC-TAMRA (SEQ ID NO:54).--

Please insert the accompanying paper copy of the Sequence Listing, page numbers 1 to 25, at the end of the application.

REMARKS

Applicants request entry of this amendment in adherence with 37 C.F.R. §§1.821 to 1.825. This amendment is accompanied by a floppy disk containing the above named sequences, SEQ ID NOS:1-54, in computer readable form, and a paper copy of the sequence information which has been printed from the floppy disk.

The information contained in the computer readable disk was prepared through the use of the software program "PatentIn" and is identical to that of the paper copy. This amendment contains no new matter.

Attached hereto is a marked-up version of the changes made to the Specification by the current Amendment. The attached pages are captioned "**VERSION WITH MARKINGS TO SHOW CHANGES MADE**".

If the Examiner believes a telephone conference would expedite prosecution of this application, please telephone the undersigned at 415-576-0200.

Respectfully submitted,

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VERSION WITH MARKINGS TO SHOW CHANGES MADE

In the Specification:

Paragraph **[35]** beginning at line 2 of page 9 has been amended as follows:

[35] FIG. 1 sets forth an amino acid sequence alignment between TGR342 (MCHr2; SEQ ID NO:2), melanin-concentrating hormone receptor (MCHr1; SEQ ID NO:19) and somatostatin receptor 1(SSTR1; SEQ ID NO:20). The arrow indicates the end of the putative truncated form of TGR342 that results from alternative splicing.

Paragraph **[66]** beginning at line 25 of page 14 has been amended as follows:

[66] The terms "GPCR" and "TGR-342, -60, -346, -and 399" therefore refer to polymorphic variants, alleles, mutants, and interspecies homologs and GPCR domains thereof that: (1) have about 70% amino acid sequence identity, preferably about 75, 80, 85, 90 or 95% or higher amino acid sequence identity, to SEQ ID NO:2,; SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:8, SEQ ID NO:10, SEQ ID NO:12, SEQ ID NO:16, or SEQ ID NO:18 over a window of about 25 amino acids, preferably 50-100 amino acids; (2) bind to antibodies raised against an immunogen comprising an amino acid sequence of SEQ ID NO:2,; SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:8, SEQ ID NO:10, SEQ ID NO:12, SEQ ID NO:16, or SEQ ID NO:18 and conservatively modified variants thereof; (3) specifically hybridize (with a size of at least about 100, preferably at least about 500 or 1000 nucleotides) under stringent hybridization conditions to a sequence SEQ ID NO:1,; SEQ ID NO:3, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:15, or SEQ ID NO:17, and conservatively modified variants thereof; or (4) have a nucleic acid sequence that has greater than about 95%, preferably greater than

about 96%, 97%, 98%, 99%, or higher nucleotide sequence identity, preferably over a region of at least about 50, 100, 200, 500, 1000, or more nucleotides, to SEQ ID NO:1~~,~~; SEQ ID NO:3, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:15, or SEQ ID NO:17; (5) are amplified by primers that specifically hybridize under stringent conditions to ~~SEQ ID NO:~~ SEQ ID NO:1~~,~~; SEQ ID NO:3, SEQ ID NO:5, SEQ ID NO:7, SEQ ID NO:9, SEQ ID NO:11, SEQ ID NO:15, or SEQ ID NO:17. This term also refers to a domain of a GPCR, as described above, or a fusion protein comprising a domain of a GPCR linked to a heterologous protein. A TGR-342, -60, -346, or -339 protein or domain typically comprises 10, 15, often 20, 25, or 30 or more contiguous amino acids of SEQ ID NOS:2~~, SEQ ID NO:2,~~ 4, 6, 8, 10, or 12. A TGR-342, -60, -346, or TGR-339 nucleic acid typically comprises at least 15, often 20, 25, 30, or 50 or more contiguous nucleotides of a sequence of SEQ ID NOS:1~~, SEQ ID NOs: 1,~~ 3, 5, 7, or 9. GPCR polynucleotide or polypeptide sequence of the invention is typically from a mammal including, but not limited to, human, rat, mouse, hamster, cow, pig, horse, sheep, or any mammal. A "TGR-342, -60, -346, and -339 polynucleotide" and a "TGR-342, -60, -346, and –339 polypeptide," are both either naturally occurring or recombinant.

Paragraph **[115]** beginning at line 3 of page 29 has been amended as follows:

[115] Nucleic acids encoding GPCRs can also be isolated from expression libraries using antibodies as probes. Such polyclonal or monoclonal antibodies can be raised using the sequence of SEQ ID NO:2; SEQ ID NO:4, SEQ ID NO:6, SEQ ID NO:8, SEQ ID NO:10, SEQ ID NO:12~~, SEQ ID NO:112,~~ SEQ ID NO:16, or SEQ ID NO:18.

Paragraph **[197]** beginning at line 17 of page 52 has been amended as follows:

[197] Common linkers such as peptides, polyethers, and the like can also serve as tags, and include polypeptide sequences, such as poly-Gly ~~poly-gly~~ sequences of between about 5 and 200 amino acids (SEQ ID NO:21). Such flexible linkers are known to persons of skill in the art. For example, poly(ethelyne glycol) linkers are available from Shearwater Polymers, Inc. Huntsville, Alabama. These linkers optionally have amide linkages, sulfhydryl linkages, or heterofunctional linkages.

Paragraphs **[243]** and **[244]** beginning at line 27 of page 65 has been amended as follows:

[243] TGR342Left primer – 5' GGAAAGTCCACGAACAATGAA 3' (SEQ ID NO:22)

[244] TGR342Right primer 5' TGAATAAGAAAAGGCATTCCAAC 3' (SEQ ID NO:23).

Paragraph **[246]** beginning at line 1 of page 66 has been amended as follows:

[246] In addition, Northern (Clontech 12-lane normal human tissue mRNA blot) and dot hybridization (Clontech multiple human tissue mRNA array blot) analyses were performed. The probe used for the northern was a 0.9 kb 3'RACE-PCR product. The sequences of the primers are as follows: Left primer: 5' CCAGTGTGGTAGATACAG TCATCCTCCCTTC 3' (SEQ ID NO:24); Right primer (AP1 from Clontech): 5' ACTCACTATAGGGC TCGAGCGGC 3' (SEQ ID NO:25).

Paragraph **[256]** beginning at line 5 of page 69 has been amended as follows:

[256] Two novel TGR60 GPCRs were also identified. The cDNA sequence of the two cDNAs are provided in SEQ ID NO:7 and SEQ ID NO:9. The

cDNAs were isolated using PCR with the following primers. TGR60L: Fwd, 5'-CACCATGCCAGCCAACTTCACAGAGGGCAGC-3' (SEQ ID NO:26); Rev, 5'-CTAGATGAA TTCTGGCTTGGACAG-3' (SEQ ID NO:27); TGR60S: Fwd, 5'-CACCATGCCAGCCAACTTCACAGA GGGCAGC-3' (SEQ ID NO:28); Rev, 5'-CTAGTCATTTCCATCTATGATCCTGCA-3' (SEQ ID NO:29).

Paragraph **[257]** beginning at line 11 of page 69 has been amended as follows:

[257] The two proteins are generated by alternative splicing of an mRNA. Expression of TGR60 was analyzed by PCR using the following primers:TGR60: Forward primer, 5'-CTGGAGCCTGTC TTTTCTGTTCTCC-3' (SEQ ID NO:30); and Reverse primer, 5'-GGCAGGTTCTGAATGATCAC AGAGG-3' (SEQ ID NO:31). The results show that TGR60 is expressed in the retina and hypothalamus (FIG. 9).

Paragraph **[259]** beginning at line 22 of page 69 has been amended as follows:

[259] The novel CG6111 nucleic acid sequence was identified by searching GenBank using the human TGR60 sequence as a query. A cDNA was isolated from adult flies and larva using PCR (Forward primer: 5' ATGAAATGTGACCACACTTTGTTC 3' (SEQ ID NO:32); Reverse primer: 5' TGCCTTCACAGGATGTCCGTGTTC 3' (SEQ ID NO:33)). Sequence analysis of the Drosophila cDNA showed differences relative to the CG6111 sequence set forth in the Celera fly genome project, which was derived from computer prediction of the sequence. The differences in the nucleic acid and protein sequences are indicated by large font, bolded, underlined characters in the sequences set forth in SEQ ID NOS:11, ~~SEQ ID NOs:11,~~ 12, 13, and 14. The DNA sequences differ by a single nucleotide at the indicated positions, and at their 3' ends (see, SEQ ID NOS:11 ~~SEQ ID NOs:11~~ and 13). The protein sequences differ at the carboxy terminus: the CG6111 protein sequence

(SEQ ID NO:14) encoded by the nucleic acid sequence identified in the fly genome project includes the amino acid sequence RRGVSLKGNTDIL (SEQ ID NO:34) at the carboxy terminus, whereas the protein encoded by the cDNA has a V residue at the carboxy terminus (SEQ ID NO:12) instead of the RRGVSLKGNTDIL (SEQ ID NO:34) sequence.

Paragraph **[263]** beginning at line 24 of page 70 has been amended as follows:

[263] A 2.4 kb transcript has been detected in several human tissue including brain, kidney, liver, lung, placenta, adipose, spleen, lymph node, thymus, bone marrow, and fetal liver. The probe used for the northern is a 505 bp PCR product. The sequences of the primer are as follows:

TGR339Left primer -- 5'ATCCCCTTCAATGTGTCCTC 3' (SEQ ID NO:35)

TGR339Right primer -- 5' GCAGTAGCCCCAGGTAGTGT 3' (SEQ ID NO:36).

Paragraph **[264]** beginning at line 30 of page 70 has been amended as follows:

[264] TGR346 was also identified from genomic sequences by searching the public databases. It is available under the accession number AC068256 (Genbank). It is 32% identical to NY2R_HUMAN (SWISS-PROT) (neuropeptide Y receptor 2) over 316 amino acids, and 31% identical to NP_004876 (Genbank) (HLWAR77, receptor for NPAF and NPAFF neuropeptides) over 291 amino acids. The primers used for PCR expression profiling are as follows:

TGR346Left -- 5' GCTTTCACAATGCTAGGTGAGG 3' (SEQ ID NO:37)

TGR346Right -- 5' AGCAAGATGTCGTTTGAGCTTT 3' (SEQ ID NO:38).

Paragraph **[266]** beginning at line 8 of page 71 has been amended as follows:

[266] Two novel mouse TGR346 nucleic acid sequences were also identified. These sequences were first identified by using the human sequence to search the mouse genome. Two genes were identified and the cDNAs subsequently isolated from mouse brain using PCR. The two mouse proteins share 73% identity. The protein mTGR346a is 83% identical to human TGR346 and mTGR346b is 77% identical to human TGR346.

Primers for FLcloning:

ms346a

Fwd: 5'-CACCATGCAGGCGCTCAACATCACCGC-3' (SEQ ID NO:39)

Rev: 5'-TTACAGTTCATGTCCACTGCCGAAAGTA-3' (SEQ ID NO:40)

ms346b

Fwd: 5'-CACCATGTCGTGGAACTTGACCGCGGA-3' (SEQ ID NO:41)

Rev: 5'-CTAAAGAGGACAAGATGCCACTTTTGA-3' (SEQ ID NO:42)

Primers for RACE:

ms346a

RACE1 5'-GCTCTTTGGCAACTCTCTGGTCATC-3' (SEQ ID NO:43)

RACE2 5' GCACGTACAACGCCTCGAGATTAAG-3' (SEQ ID NO:44)

RACE3 5'-ACCTTCATCCTCGTCATCCTCTTCC-3' (SEQ ID NO:45)

ms346b

RACE1 5'-ACGCCCTGGTAGTCTATGTGGTGAC-3' (SEQ ID NO:46)

RACE2 5'-TGCACCAGAAGATCTACACCACCTTC-3' (SEQ ID NO:47)

RACE3 5'-ATTCTTGGCACCCTCTTCCTGCTAC-3' (SEQ ID NO:48)

Paragraph **[267]** beginning at line 8 of page 71 has been amended as follows:

[267] Expression of the two genes was analyzed by QPCR. Primers for analysis of ms346a expression were: Fwd, 5' AAGGCAACTCAAGCGACAGC 3' (SEQ ID NO:49); and Rev, 5'CAAATGA TATTAGCTATGAGGATATCATTACA (SEQ ID NO:50). The probe was 6FAM-CTGAAAACTCTACTTTCGGCAGTGGACATGA-TAMRA (SEQ ID NO:51). The QPCR primers to analyze ms346b expression were: Fwd, 5' TCTTGTCCTCTTTAGTTCCGAATTTC 3' (SEQ ID NO:52); Rev, 5' TTCGATTACAGTATGACAGATACTCATTCT 3' (SEQ ID NO:53). The probe was 6FAM-CTCTGCTGTAGACGTGAACACTGTACCAATGTC-TAMRA (SEQ ID NO:54).